

PATENT

E UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.:

10/694,634

Applicant:

Tan et al.

Filed:

October 27, 2003

TC/A.AU.:

1633

Examiner:

Ileana Popa

Docket No.:

12062.105020 (RSK020)

Customer No.:

20786

Title:

Methods and compounds for disruption of CD40R/CD40L signaling in the treatment

Confirmation No.: 2636

of Alzheimer's disease

Mail Stop Amendment Commissioner for Patents P. O. Box 1450 Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

The citation of information on the accompanying Form PTO/SB/08A, "Information Disclosure Statement by Applicant" is made pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98. A copy of each cited reference is enclosed except for U.S. Patents and U.S. Patent Application Publications. The Examiner's attention is also drawn to U.S. Patent Application No. 11/523,468. The citation of this information does not constitute an admission of priority or that any cited item is available as a reference, or a waiver of any right the applicant may have under applicable statutes, Rules of Practice in patent cases, or otherwise.

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Respectfully submitted,

Dated: May 17, 2007

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449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 11

Complete if Known					
Application Number	10/694,634				
Filing Date	October 27, 2003				
First Named Inventor	Tan et al.				
Group Art Unit	1633				
Examiner Name	Ileana Popa				
Attorney Docket Number	12062.105020 (RSK020)				

		· · · · · · · · · · · · · · · · · · ·	U.	S. PATENT DOCUMENTS		
Examiner Initials *	Cite No. 1	*	ent Kind Code if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages/Relevant Figures Appear
	AA	3,791,932	A	Schuurs et al.	02-12-1974	
	AB	3,839,153	Α	Schuurs et al.	10-01-1974	
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	AAF	5,175,384	Α	Krimpenfort et al.	12-29-1992	

Examiner	Date	
Signature	 Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Complete if Known Substitute for form 1449A/PTO **Application Number** 10/694,634 Filing Date October 27, 2003 INFORMATION DISCLOSURE First Named Inventor Tan et al. STATEMENT BY APPLICANT Group Art Unit 1633 (use as many sheets as necessary) **Examiner Name** Ileana Popa Attorney Docket Number 12062.105020 (RSK020) 11 Sheet

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			Ū.	S. PATENT DOCUMENTS		
Examiner Initials *	Cite No. 1	U.S. Patent Docum Number	ent Kind Code if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages/Relevant Figures Appear
	BA	5,175,385	A	Wagner et al.	12-29-1992	
	BB	5,192,659	Α	Simons	03-09-1993	
	BC	5,221,778	Α	Byrne et al.	06-22-1993	
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				FC	PREIGN PATENT DOCUMENTS			
Examiner Initials *	Cite No. ¹		ign Patent Docum Number Kind Cod (if known	le ²	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages- Relevant Figures Appear	T ⁶
	CA	wo	93/14200	A1	TSI Corporation	07-22-1993		Ι
	СВ	wo	94/06908	A1	Regents of Univ. California	03-31-1994		
	CC	wo	94/23049	A2	Johns Hopkins University	10-13-1994		
	CD	WO	94/28123	A1	Ontario Cancer Institute	12-08-1994		
	CE	wo	97/32016	A1	Ohio State Research Foundation	09-04-1997		
	CF	wo	00/23590	A2	Georgetown Univ. Med. Center	04-27-2000		
	CG	wo	01/96397	A2	Biogen Inc.	12-20-2001		

		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	СН	AUGUST, J., et al., Eds., Gene Therapy (Advances in Pharmacology, Vol. 40) (Academic Press, San Diego, Calif., 1997, ISSN 1054-3589), table of contents.	
	CI	ARCH, R.H., et al., "Tumor necrosis factor receptor-associated factors (TRAFs)a family of adapter proteins that regulates life and death," Genes Dev., 12(18):2821-2830 (September 15, 1998).	
	Cl	AUSUBEL, F.M., et al., Eds., Current Protocols in Molecular Biology (John WIley and Sons, Baltimore, Maryland, 1989), table of contents.	
	CK	BACSKAI, B.J., et al., "Imaging of amyloid-beta deposits in brains of living mice permits direct observation of clearance of plaques with immunotherapy," <i>Nature Med.</i> , 7(3):369-372 (March 2001).	
	CL	BALL, M.J., et al., "A new definition of Alzheimer's disease: a hippocampal dementia," Lancet, 1(8419):14-16 (January 5, 1985).	
	СМ	BARD, F., et al., "Peripherally administered antibodies against amyloid beta-peptide enter the central nervous system and reduce pathology in a mouse model of Alzheimer disease," <i>Nature Med.</i> , 6(8):916-919 (August 2000).	
	CN	BARGER, S.W., and HARMON, A.D., "Microglial activation by Alzheimer amyloid precursor protein and modulation by apolipoprotein E," <i>Nature</i> , 388(6645):878-881 (August 28, 1997).	
	со	BIRREN et al (eds), Genome Analysis: A Laboratory Manual Series, Vols. 1-4 (Cold Spring Harbor Laboratory Press, New York, 1998), table of contents.	
	СР	BLOCK, M.L., and HONG, J.S., "Microglia and inflammation-mediated neurodegeneration: multiple triggers with a common mechanism," <i>Prog. Neurobiol.</i> , 76(2):77-98 (June 2005).	
	CQ	BORREBAECK, C.A.K., Ed., Antibody EngineeringA Practical Guide (W.H. Freeman and Co., 1992), table of contents.	

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Substitute	for form 1449A/PTO		Application Number	10/694,634	
INFO	DRMATION D	ISCLOSURE	Filing Date	October 27, 2003	
STA	TEMENT BY A	APPLICANT	First Named Inventor	Tan et al.	
~			Group Art Unit	1633	
	(use as many sheets o	is necessary)	Examiner Name	Ileana Popa	
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		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
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	DA	BURKE, D.T., and OLSON, M.V., "Preparation of clone libraries in yeast artificial-chromosome vectors," Chap. 17 in Methods in Enzymology, Vol. 194: Guide to Yeast Genetics and Molecular Biology, (Academic Press) pp. 251-270 (1991).	
	DB	CALINGASAN, N.Y., et al., "Identification of CD40 ligand in Alzheimer's disease and in animal models of Alzheimer's disease and brain injury," <i>Neurobiol. Aging</i> , 23(1):31-39 (January-February 2002).	
	DC	CAPECCHI, M.R., "Altering the genomeby homologous recombination," <i>Science</i> , 244(4910):1288-1292 (June 16, 1989).	
	DD	CARSON, M.J., et al., "Mature microglia resemble immature antigen-presenting cells," Glia, 22(1):72-85 (January 1998).	
	DE	CASTILLO, G.M., et al., "Perlecan binds to the beta-amyloid proteins (A beta) of Alzheimer's disease, accelerates A beta fibril formation, and maintains A beta fibril stability," J. Neurochem. 69(6):2452-2465 (December 1997).	
	DF	CHANG et al., Somatic Gene Therapy, CRC Press, Ann Arbor, MI (1995), table of contents.	
	DG	COMBS, C.K., et al., "Identification of microglial signal transduction pathways mediating a neurotoxic response to amyloidogenic fragments of beta-amyloid and prion proteins," J. Neurosci., 19(3):928-939 (February 1, 1999).	
	DH	DAVIES, N.P., et al., "Targeted alterations in yeast artificial chromosomes for inter-species gene transfer," Nucleic Acids Res., 20(11):2693-2698 (June 11, 1992).	
	DI	DeMATTOS, R.B., et al., "Brain to plasma amyloid-β efflux: a measure of brain amyloid burden in a mouse model of Alzheimer's disease," Science, 295(5563):2264-2267 (March 22, 2002).	
	DJ	DeMATTOS, R.B., et al., "Peripheral anti-A beta antibody alters CNS and plasma Aβ clearance and decreases brain Aβ burden in a mouse model of Alzheimer's disease," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 98(15):8850-8855 (July 17, 2001) (Electronic publication July 3, 2001).	
	DK	DENFELD, R.W., et al., "CD40 is functionally expressed on human keratinocytes," Eur. J. Immunol., 26(10):2329-2334 (October 1996).	
	DL	DICKINSON, P., et al., "High frequency gene targeting using insertional vectors," Hum. Mol. Genet., 2(8):1299-1302 (August 1993).	
	DM	DING, S.W., "RNA silencing," Curr. Opin. Biotechnol., 11(2):152-156 (April 2000).	
	DN	DUFF, K., and LINCOLN, S., "Insertion of a pathogenic mutation into a yeast artificial chromosome containing the human APP gen and expression in ES cells," Chap. 80 in Research Advances in Alzheimer's Disease and Related Disorders, Iqbal, K., et al., (Eds.) (John Wiley & Sons, 1995).	
	DO	ELLIS, R. J., et al., "Cerebral amyloid angiopathy in the brains of patients with Alzheimer's disease: the CERAD experience, Part XV," Neurology, 46(6):1592-1596 (June 1996).	

Signature Considered		
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Cutations	for form 1449A/PTO		Complete if Known		
Substitute	: for form 1449A/PTO		Application Number	10/694,634	
INFO	DRMATION D	ISCLOSURE	Filing Date	October 27, 2003	
STA'	TEMENT BY	APPLICANT	First Named Inventor	Tan et al.	
		,	Group Art Unit	1633	
	(use as many sheets	as necessary)	Examiner Name	Ileana Popa	
Sheet	Sheet 5 11		Attorney Docket Number	12062.105020 (RSK020)	

		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
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	EA	FOY, T.M., et al., "Immune regulation by CD40 and its ligand GP39," Annu. Rev. Immunol., 14:591-617 (1996).	
	EB	FRACKOWIAK, J., et al., "Ultrastructure of the microglia that phagocytose amyloid and the microglia that produce beta-amyloid fibrils," Acta Neuropathol. (Berl)., 84(3):225-233 (1992).	
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	EE	GREWAL, T.S., et al., "Requirement for CD40 ligand in costimulation induction, T cell activation, and experimental allergic encephalomyelitis," <i>Science</i> , 273(5283):1864-1867 (September 27, 1996).	
	EF	GRIBSKOV, M., and DEVEREAUX, G., <u>Sequence Analysis Primer</u> , (Stockton Press, 1991) table of contents.	
	EG	HAMILTON, A.J., and BAULCOMBE, D.C., "A species of small antisense RNA in posttranscriptional gene silencing in plants," <i>Science</i> , 286(5441):950-952 (October 29, 1999).	
	ЕН	HARLOW, E., and LANE, D., Chapter 5, "Immunizations," in <u>Antibodies: A Laboratory Manual</u> (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988), pp. 53-59.	
	EI	HARRIS-WHITE, M.E., <i>et al.</i> , "Effects of transforming growth factor-β (isoforms 1-3) on amyloid-β deposition, inflammation, and cell targeting in organotypic hippocampal slice cultures," <i>J. Neurosci.</i> , 18(24):10366-10374. (December 15, 1998).	
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	EL	HOLCOMB, L., et al., "Accelerated Alzheimer-type phenotype in transgenic mice carrying both mutant amyloid precursor protein and presenilin 1 transgenes," <i>Nature Med.</i> , 4(1):97-100 (January 1998).	
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	EN	HSIAO, K., et al., "Correlative memory deficits, Abeta elevation, and amyloid plaques in transgenic mice," Science, 274(5284):99-102 (October 4, 1996).	
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	EP	HUBERMAN, M. et al., "Correlation of cytokine secretion by mononuclear cells of Alzheimer patients and their disease stage," J. Neuroimmunol., 52(2):147-152 (July 1994).	

	18 to 11 to 2		
Examiner		Date	
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Calbaria	Substitute for form 1449A/PTO			Complete if Known
Substitute	e for form 1449A/PTO		Application Number	10/694,634
INFO	DRMATION D	ISCLOSURE	Filing Date	October 27, 2003
STA'	TEMENT BY	APPLICANT	First Named Inventor	Tan et al.
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	FA	HUNTER, C.P., "Genetics: a touch of elegance with RNAi," Curr. Biol., 9(12):R440-R442 (June 17, 1999).	
	FB	HUSTON, J.S., et al., "Protein engineering of single-chain Fv analogs and fusion proteins," Methods Enzymol., 203:46-88 (1991).	
	FC	HUXLEY, C., et al., "The human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion," Genomics, 9(4):742-50 (April 1991).	
	FD	INNIS, M.A., et al., Eds., PCR Protocols: A Guide To Methods And Applications, Academic Press, San Diego, CA (1990) table of contents.	
	FE	IRIZARRY, M.C., et al., "APPSw transgenic mice develop age-related A beta deposits and neuropil abnormalities, but no neuronal loss in CA1," J. Neuropathol. Exp. Neurol., 56(9):965-973 (September 1997).	
	FF	IWATSUBO, T., et al., "Visualization of Aβ42(43) and Aβ40 in senile plaques with end-specific Ab monoclonals: evidence that an initially deposited species is Aβ42(43)<" Neuron, 13(1):45-53 (July 1994).	
	FG	JAKOBOVITS, A., et al., "Germ-line transmission and expression of a human-derived yeast artificial chromosome," <i>Nature</i> , 362(6417):255-255 (March 18, 1993).	
	fН	JAMES, N.D., et al., "Neurodegenerative changes including altered tau phosphorylation and neurofilament immunoreactivity in mice transgenic for the serine/threonine kinase Mos.," Neurobiol. Aging, 17(2), 235-241 (March-April 1996).	
	FI	JANUS, C., et al., "Aβ peptide immunization reduces behavioural impairment and plaques in a model of Alzheimer's disease," Nature,;408(6815):979-982 (December 21-28, 2000).	
	FJ	JARRETT, J.T., et al., "Seeding "one-dimensional crystallization" of amyloid: a pathogenic mechanism in Alzheimer's disease and scrapie?" Cell, 73(6):1055-1058 (June 18, 1993).	
	FK	JARRETT, J.T., et al., "The carboxy terminus of the β amyloid protein is critical for the seeding of amyloid formation: implications for the pathogenesis of Alzheimer's disease," Biochemistry, 32(18):4693-4697 (May 11, 1993).	
	FL	JOHNSON, S., and BIRD, R.E., "Construction of single-chain Fv derivatives monoclonal antibodies and their production in <i>Escherichia coli</i> ," <i>Meth. Enzymol.</i> , 203:88-98 (1991).	
	FM	JOHNSON-WOOD, K., et al., "Amyloid precursor protein processing and A beta42 deposition in a transgenic mouse model of Alzheimer disease," Proc. Natl. Acad. Sci. U.S.A., 94(4):1550-1555 (February 18, 1997).	
Ē	FN	JOHNSTONE, A., and THORPE, R., <u>Immunochemistry in Practice</u> , 2 nd Ed. (Blackwell Scientific Publications, Boston, 1982), table of contents.	

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Substitute for form 1449A/PTO			Application Number	10/694,634
INFO	RMATION	DISCLOSURE	Filing Date	October 27, 2003
STAT	EMENT BY	APPLICANT	First Named Inventor	Tan et al.
			Group Art Unit	1633
	(use as many shee	ets as necessary)	Examiner Name	Ileana Popa
Sheet 7 11			Attorney Docket Number	12062.105020 (RSK020)

		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	No. journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country who				
	GA	KALARIA, R.N., "Microglia and Alzheimer's disease," Curr. Opin. Hematol., 6(1):15-24 (January 1999).			
	GB	KARMANN, K., et al., "CD40 on human endothelial cells: inducibility by cytokines and functional regulation of adhesion molecule expression," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 92(10), 4342-4346 (May 9, 1995).			
	GC	KLEGERIS, A., et al., "Interaction of Alzheimer beta-amyloid peptide with the human monocytic cell line THP-1 results in a protein kinase C-dependent secretion of tumor necrosis factor-alpha," Brain Res., 747(1):114-121 (January 30, 1997).			
	GD	LAMB, B.T., et al., "Introduction and expression of the 400 kilobase amyloid precursor protein gene in transgenic mice [corrected]," Nat. Genet., 5(1):22-30 (September 1993).			
	GE	LAWRENCE, C.W., "Classical Mutagenesis Techniques," Chapter 17 in Methods in Enzymology, Vol. 194: Guide to Yeast Genetics and Molecular Biology, (Academic Press) pp. 273-281 (1991).			
	GF	LI, Q.X. et al., "Membrane-associated forms of the beta A4 amyloid protein precursor of Alzheimer's disease in human platelet and brain: surface expression on the activated human platelet," Blood, 84(1):133-142 (July 1, 1994).			
	GG	LIM, G.P., et al., "Ibuprofen suppresses plaque pathology and inflammation in a mouse model for Alzheimer's Disease," J. Neurosci., 20(15):5709-5714 (August 1, 2000).			
	GH	LUO, Y., et al., "Mice deficient in BACE1, the Alzheimer's beta-secretase, have normal phenotype and abolished beta-amyloid generation," Nat. Neurosci., 4(3):231-232 (March 2001).			
	GI	LUTGENS, E., et al., "Requirement for CD154 in the progression of atherosclerosis," Nature Med., 5(11):1313-1316 (November 1999).			
	Gì	MACH, F., et al., "Functional CD40 ligand is expressed on human vascular endothelial cells, smooth muscle cells, and macrophages: implications for CD40-CD40 ligand signaling in atherosclerosis," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 94(5):1931-1936 (March 4, 1997).			
	GK	MacKENZIE, I.R., and MUNOZ, D.G., et al., "Nonsteroidal anti-inflammatory drug use and Alzheimer-type pathology in aging," Neurology, 50(4):986-990 (April 1998).			
	GL	MARSHAK, D.R., et al, Strategies for Protein Purification and Characterization. A laboratory course manual, CSHL Press, 1996, table of contents.			
	GM	McGEER, E.G., and McGEER, P.L., "The importance of inflammatory mechanisms in Alzheimer disease," Exper. Geriontol., 33(5):371-378 (August 1998).			
	GN	McGEER, P.L., and McGEER, E.G., "Inflammation of the brain in Alzheimer's disease: implications for therapy," J. Leukocyte Biol., 65(4):409-415 (April 1999).			
	GO	MEDA L., et al., "Proinflammatory profile of cytokine production by human monocytes and murine microglia stimulated with beta-amyloid[25-35]," J. Neuroimmunol., 93(1-2):45-52 (January 1, 1999).			

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	НА	MEDA. L., et al., "Activation of microglial cells by beta-amyloid and interferon-gamma," Nature, 374(6523): 647-650 (April 13, 1995).	
	нв	MERNAUGH, R., and MERNAUGH, G., "An overview of phage-displayed recombinant antibodies," Chap. 25 in Molecular Methods in Plant Pathology, Singh, R.P., and Sing, U.S., Eds. (CRC Press, Boca Raton, Fla., 1995), ISSN 0-87371-877-1), pp. 359-365.	
	нс	MISHELL and SHIIGI (eds), Selected Methods in Cellular Immunology, W.H. Freeman and Co., New York (1980) table of contents.	
	HD	MORGAN, D., et al., "Aβ peptide vaccination prevents memory loss in an animal model of Alzheimer's disease," <i>Nature</i> , 408(6815):982-985 (December 21-28, 2000).	
	HE	NGUYEN, V.T., et al., "Post-transcriptional inhibition of CD40 gene expression in microglia by transforming growth factor-□," Eur. J. Immunol., 28(8):2537-2548, (August 1998).	
	HF	NI, C.Z., et al., "Molecular basis for CD40 signaling mediated by TRAF3," Proc. Natl. Acad. Sci. U.S.A., 97(19):10395-10399 (September 12, 2000).	
	НG	NILSSON, L.N., et al., "Alpha-1-antichymotrypsin promotes beta-sheet amyloid plaque deposition in a transgenic mouse model of Alzheimer's disease," J. Neurosci., 21(5):1444-1451 (March 1, 2001).	
	нн	OLEANA, V.H., et al., "Increased expression of the TIAR protein in the hippocampus of Alzheimer patients," Neuroreport, 9(7):1451-1454 (May 11, 1998).	
	ні	OPPENHEIM, J.J., et al., "Cytokines," Chap. 9 in <u>Basic and Clinical Immunology (8th Edition)</u> , Stites, D.P., Terr, A.I., and Parslow, T.G., Eds., Appleton & Lange, Norwalk, Conn., 1994), pp. 105-123.	
	НЈ	PEARSON, B.E., and CHOI, T.K., "Expression of the human beta-amyloid precursor protein gene from a yeast artificial chromosome in transgenic mice," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 90(22):10578-10582 (November 15, 1993).	
	нк	PERBAL, A Practical Guide to Molecular Cloning, John Wiley & Sons, New York (1988), table of contents.	
	HL	PIGUET, P.F., et al., "Role of CD40-CVD40L in mouse severe malaria," Amer. J. Pathol., 159(2):733-742 (August 2001).	
	НМ	PULLEN, S.S., et al., "CD40-tumor necrosis factor receptor-associated factor (TRAF) interactions: regulation of CD40 signaling through multiple TRAF binding sites and TRAF hetero-oligomerization," <i>Biochemistry</i> , 37(34):11836-11845 (August 25, 1998).	
	HN	RAM, Z., CULVER, K.W., et al., "Therapy of malignant brain tumors by intratumoral implantation of retroviral vector-producing cells," Nat. Med., 3(12):1354-1361 (December 1997).	
	НО	RODRIGUEZ, R.L., and DENHARDT, D.T., Eds., "Vectors: A Survey of Molecular Cloning Vectors and Their Uses," <i>Biotechnology</i> , 10:1-578 (1988), <i>table of contents</i> .	

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Examiner	Date	
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7.1	C C 1440 1 /DTO		· · ·	Complete if Known
Substitute	for form 1449A/PTO		Application Number	10/694,634
INF	DRMATION D	ISCLOSURE	Filing Date	October 27, 2003
STA'	TEMENT BY	APPLICANT	First Named Inventor	Tan et al.
			Group Art Unit	1633
	(use as many sheets	as necessary)	Examiner Name	Ileana Popa
Sheet	9	11	Attorney Docket Number	12062.105020 (RSK020)

		OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No. '	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	IA	ROGERS, J., et al., "Expression of immune system-associated antigens by cells of the human central nervous system: relationship to the pathology of Alzheimer's disease," Neurobiol. Aging, 9(4):339-349 (July-August 1988).	
	IB	ROGERS, J., et al., "Inflammation and Alzheimer's disease pathogenesis," Neurobiol. Aging, 17(5):681-686 (September-October 1996).	
	IC	ROGERS, J., and ROVIGATTI, U., "Immunologic and tissue culture approaches to the neurobiology of aging." <i>Neurobiol. Aging</i> , 9(5-6):759-762 (September-December 1988).	
	ID	ROTHSTEIN, R., "Targeting, disruption, replacement, and allele rescue: integrative DNA transformation in yeast," Chap. 19 in Methods in Enzymology, Vol. 194: Guide to Yeast Genetics and Molecular Biology, (Academic Press) pp. 281-301 (1991).	
	IE	ROZEMULLER, J.M., et al., "A4 protein in Alzheimer's disease: primary and secondary cellular events in extracellular amyloid deposition," J. Neuropathol. Exp. Neurol., 48(6):674-691 (November 1989).	
	IF	RUGGIERO, G., et al., "CD40 expressed on thymic epithelial cells provides costimulation for proliferation but not for apoptosis of human thymocytes," J. Immunol., 156(10):3737-3746 (May 15, 1996).	
	IG	SAMBROOK, J., et al., "Analysis of Genomic DNA by Southern Hybridization," Molecular Cloning: <u>A Laboratory Manual</u> , 2d. Ed., (Cold Spring Harbor Laboratory Press, New York, 1989), pp. 9.31-9.57 and pp. 18.60-18.75.	
	IH	SCHEDL, A., et al., "A yeast artificial chromosome covering the tyrosinase gene confers copy number-dependent expression in transgenic mice," <i>Nature</i> , 362(6417):258-261 (March 18, 1993).	
	II	SCHENK, D., et al., "Immunization with amyloid-β attenuates Alzheimer-disease-like pathology in the PDAPP mouse," <i>Nature</i> , 400(6740):173-177 (July 8, 1999).	
	IJ	SCHMIDT, M.L., et al., "Relative abundance of tau and neurofilament epitopes in hippocampal neurofibrillary tangles," Am. J. Pathol., 136(5):1069-1075 (May 1990).	
	IK	SCHNEIDER, A., et al., "Phosphorylation that detaches tau protein from microtubules (Ser262, Ser214) also protects it against aggregation into Alzheimer paired helical filaments," <i>Biochemistry</i> , 38(12):3549-3558 (March 23, 1999).	
	IL	SCHÖNBECK, U., et al., "Inhibition of CD40 signaling limits evolution of established atherosclerosis in mice," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 97(13):7458-7463 (June 20, 2000).	
	IM	SCHÖNBECK, U., et al., "Ligation of CD40 activates interleukin 1 β-converting enzyme (caspase-1) activity in vascular smooth muscle and endothelial cells and promotes elaboration of active interleukin 1 β," J. Biol. Chem., 272(31):19569-19574 (August 1, 1997).	
	IN	SCHÖNBECK, U., et al., "The CD40/CD154 receptor/ligand dyad," Cell Mol. Life Sci., 58(1):4-43 (January 2001).	

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	JA	SEMPOWSKI, G.D., et al., "CD40 is a functional activation antigen and B7-independent T cell costimulatory molecule on normal human lung fibroblasts," <i>J. Immunol.</i> , 158(10): 4670-4677 (May 15, 1997).	
	JB	SEUBERT, P., et al., "Isolation and quantification of soluble Alzheimer's β-peptide from biological fluids," Nature, 359(6393):325-327 (September 24, 1992).	
	ìC	SIKORSKI, R.S., and BOEKE, J.D., "In vitro mutagenesis and plasmid shuffling: from cloned gene to mutant yeast," Chap. 20 in Methods in Enzymology, Vol. 194: Guide to Yeast Genetics and Molecular Biology, (Academic Press) pp. 302-318.	
	JD	STEWART, W.F., et al., "Risk of Alzheimer's disease and duration of NSAID use," Neurology, 48(3):626-632 (March 1997).	
. "	JE	STOUT, R.D., and SUTTLES, J., "The many roles of CD40 in cell-mediated inflammatory responses," <i>Immunology Today</i> , 17(10):487-492 (October 1996).	
	JF	STRAUSS, W.M., et al., "Germ line transmission of a yeast artificial chromosome spanning the murine alpha 1(I) collagen locus," Science, 259(5103):1904-1907 (March 26, 1993).	
	JG	STÜBER, E., et al., "Blocking the CD40L-CD40 interaction in vivo specifically prevents the priming of T helper 1 cells through the inhibition of interleukin 12 secretion," J. Exper. Med., 183(2):693-698 (February 1, 1996).	
	JH	STURCHLER-PIERRAT, C., et al., "Two amyloid precursor protein transgenic mouse models with Alzheimer disease-like pathology," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 94(24):13287-13292 (November 25, 1997).	
	JI	STYREN, S.D., et al., "Expression of differential immune factors in temporal cortex and cerebellum: the role of alpha-1-antichymotrypsin, apolipoprotein E, and reactive glia in the progression of Alzheimer's disease," J. Comp. Neurol., 396(4):511-520 (July 13, 1998).	
	IJ	SUO, Z., et al., "Alzheimer's β-amyloid peptides induce inflammatory cascade in human vascular cells: the roles of cytokines and CD40," Brain Res., 807(1-2):110-117 (October 5, 1998).	
	JK	TAN, J., "CD40 is expressed and functional on neuronal cells," <i>EMBO J.</i> , 21(4):643-652 (February 15, 2002).	
	JL	TAN, J., et al., "Activation of microglial cells by the CD40 pathway: relevance to multiple sclerosis," J. Neuroimmunol., 97(1-2):77-85 (June 1, 1999).	
	JM	TAN, J., et al., "Microglial activation resulting from CD40R-CD40L interaction after β-Amyloid stimulation," Science, 286(5448):2352-2355 (December 17, 1999).	
	JN	TESTONI, N., et al., "A new method of "in-cell reverse transcriptase-polymerase chain reaction" for the detection of BCR/ABL transcript in chronic myeloid leukemia patients," Blood, 87(9):3822-3827 (May 1, 1996).	

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			Filing Date	October 27, 2003		
			First Named Inventor	Tan et al.		
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			Examiner Name	Ileana Popa		
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	KA	THINAKARAN, G., et al., "Metabolism of the "Swedish" amyloid precursor protein variant in neuro2a (N2a) cells. Evidence that cleavage at the "beta-secretase" site occurs in the golgi apparatus," J. Biol. Chem., 271(16):9390-9397 (April 19, 1996).	
	КВ	TOGO, T., et al., "Expression of CD40 in the brain of Alzheimer's disease and other neurological diseases," Brain Res., 885(1):117-121 (December 1, 2000).	
	кс	UCHIHARA, T., et al., "Activated microglial cells are colocalized with perivascular deposits of amyloid-beta protein in Alzheimer's disease brain," Stroke, 28(10):1948-1950 (October 1997).	
KD VEGA, M.A., Gene Targeting, CRC Press, Ann Arbor, MI (1994), table of contents.			1
	KE	WATSON, J.; GILMAN, M.; WITKOWSKI, J.; Recombinant DNA, 2 nd Ed., (Scientific American Books, New York, 1992), table of contents.	
	KF	WEGIEL, J., et al., "Microglia cells are the driving force in fibrillar plaque formation, whereas astrocytes are a leading factor in plague degradation," Acta Neuropathol. (Berl)., 100(4):356-64 (October 2000).	
	KG	WU, D., et al., "Drug targeting of a peptide radiopharmaceutical through the primate blood-brain barrier in vivo with a monoclonal antibody to the human insulin receptor," J. Clin. Investig., 100(7):1804-1812. (October 1, 1997).	
-	КН	WYSS-CORAY, T., et al., "TGF-β1 promotes microglial amyloid-beta clearance and reduces plaque burden in transgenic mice," <i>Nature Med.</i> , 7(5):612-618 (May 2001).	
	KI	XIA, W., "Enhanced production and oligomerization of the 42-residue amyloid β-protein by Chinese hamster ovary cells stably expressing mutant presentilins," J. Biol. Chem., 272(12):7977-7982 (March 21, 1997).	
	KJ	XU, J., et al., "Mice deficient for the CD40 ligand," <i>Immunity</i> , 1(5):423-431 (August 1994). Erratum in: Immunity 1(7):following 613 (October 1994).	

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